Appendix A

1. Preparation of Amlodipine Free Base Form I

Amlodipine free base Form I was prepared as follows:

Reaction scheme:

Amlodipine free base (crude) —(1) EtOH, (2) H_2O→ Amlodipine free base Form I

Starting materials:	FW	Amount	Mol	Ratio
amlodipine free base	408.88	117 g	0.286	1

Reagents and solvents:	
ethanol	1080 ml

117 g of crude amlodipine free base was dissolved in 1080 ml of boiling ethanol. Then, 2160 ml water was added and the mixture was left to cool to room temperature. During cooling, a solid started to precipitate. The mixture was cooled on an ice-bath for 1 hour. The solid was isolated by filtration and washed with 180 ml water. The solid was dried in a vacuum oven at 40 °C.

Isolated yield: 98.2 gram (84%)

2. Preparation of Amlodipine Free Base Form II

Amlodipine free base Form II was prepared as follows:

Reaction scheme:

Amlodipine free base (crude) —(1) toluene, (2) *n*-hexane→ Amlodipine free base Form II

Starting materials:	FW	Amount	Mol	Ratio
amlodipine free base	408.88	110.5 g	0.270	1

Reagents and solvents:	
Toluene	425 ml
n-hexane	5100 ml

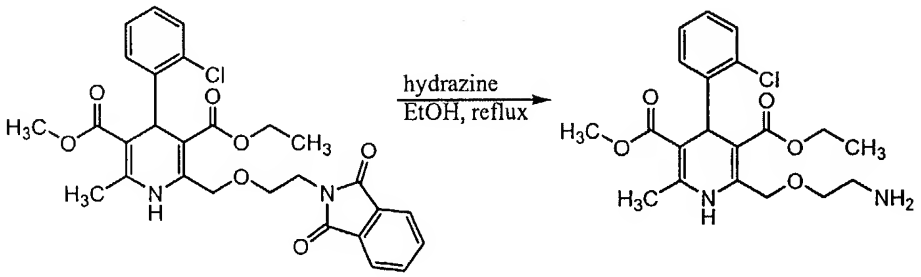
110.5 g of crude amlodipine free base was dissolved in 425 ml of boiling toluene. This solution was added slowly in 15 minutes to a 0-3 °C solution of 5100 ml *n*-hexane under stirring. During the addition, the temperature of the n-hexane solution was kept below 3 °C. The solid was filtered off and dried under vacuum at ambient temperature.

Isolated yield: 103.85 gram (94%).

3. Preparation of Amlodipine Free Base Form III

Amlodipine free base Form III was prepared as follows:

Reaction scheme:



Starting materials:	FW	Amount	Mol	Ratio
phtalodipine	538.98	191.5 g	0.355	1

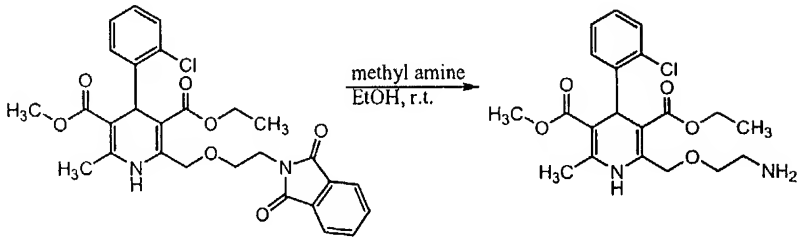
Reagents and solvents:				
Ethanol		2000 ml		
hydrazine monohydrate	50.06	53.4 g	1.067	3
dichloromethane		1000 ml		

191.5 g of phtalodipine (4-(2-chlorophenyl)-3-ethoxycarbonyl-5-methoxycarbonyl-6-methyl-2-(2-phtalimidoethoxy)methyl-1,4-dihydropyridine was stirred in 2000 ml refluxing ethanol containing 53.4 g hydrazine monohydrate. After 2 hours, the reaction mixture was cooled and filtered. The filtrate was evaporated and the residue was dissolved in 1000 ml dichloromethane and the solution was washed with 1000 ml water. The organic layer was evaporated to dryness and dried until constant weight.

Isolated yield: 116.61 gram (80 %)

4. Preparation of Amorphous Amlodipine Free Base

Reaction scheme:



Starting materials:	FW	Amount	Mol	Ratio
phtalodipine	538.98	160.0 g	0.297	1

Reagents and solvents:

33% ethanolic methyl amine	2000 ml
industrial methylated spirits	600 ml

160.0 g of phtalodipine (4-(2-chlorophenyl)-3-ethoxycarbonyl-5-methoxycarbonyl-6-methyl-2-(2-phtalimidoethoxy)methyl-1,4-dihydropyridine was stirred in 2000 ml 33% ethanolic methylamine solution at room temperature for three hours. The solvent then was evaporated and the residue was slurried in 600 ml industrial methylated spirits, and then filtered. The filtrated was concentrated at reduced pressure to dryness.

Isolated yield: about 120 g (quantitative yield).